CLAIMS

1. A method of stimulating an immune response, comprising

administering an immunostimulatory nucleic acid selected from the group consisting of a Py-rich nucleic acid and a TG nucleic acid, to a non-rodent subject in an amount effective to induce an immune response in the non-rodent subject.

2. The method of claim 1, wherein the immunostimulatory nucleic acid is a T-rich nucleic acid.

3. The method of claim 2, wherein the T-rich immunostimulatory nucleic acid is a poly T nucleic acid comprising

5′ TTTT 3'.

4. The method of claim 3, wherein the poly T nucleic acid comprises

5′ X_1 X_2TTTTX_3 X_4 3'

wherein X_1, X_2, X_3 and X_4 are nucleotides.

5. The method of claim 3, wherein the T-rich immunostimulatory nucleic acid comprises a plurality of poly T nucleic acid motifs.

6. The method of claim 4, wherein X_1X_2 is TT.

7. The method of claim 4, wherein X_3X_4 is TT.

8. The method of claim 4, wherein X_1X_2 is selected from the group consisting of TA, TG, TC, AT, AA, AG, AC, CT, CC, CA, GT, GG, GA, and GC.

9. The method of claim 4, wherein X_3X_4 is selected from the group consisting of TA, TG, TC, AT, AA, AG, AC, CT, CC, CA, GT, GG, GA, and GC.

10. The method of claim 3, wherein the T-rich immunostimulatory nucleic acid comprises a nucleotide composition of greater than 25% T.

11. The method of claim 1, wherein the T-rich immunostimulatory nucleic acid comprises a nucleotide composition of greater than 35% T.

12. The method of claim 1, wherein the T-rich immunostimulatory nucleic acid comprises a nucleotide composition of greater than 40% T.

13. The method of claim 1, wherein the T-rich immunostimulatory nucleic acid comprises a nucleotide composition of greater than 50% T.

14. The method of claim 1, wherein the T-rich immunostimulatory nucleic acid comprises a nucleotide composition of greater than 60% T.

15. The method of claim 1, wherein the T-rich immunostimulatory nucleic acid comprises a nucleotide composition of greater than 80% T.

16. The method of claim 1, wherein the immunostimulatory nucleic acid comprises at least 20 nucleotides.

17. The method of claim 1, wherein the immunostimulatory nucleic acid comprises at least 24 nucleotides.

18. The method of claim 1, wherein the immunostimulatory nucleic acid has a nucleotide backbone which includes at least one backbone modification.

19. The method of claim 18, wherein the backbone modification is a phosphorothioate modification.

20. The method of claim 18, wherein the nucleotide backbone is chimeric.

21. The method of claim 18, wherein the nucleotide backbone is entirely modified.

22. The method of claim 1, wherein the immunostimulatory nucleic acid is free of CpG dinucleotides.

23. The method of claim 1, wherein the immunostimulatory nucleic acid is free of unmethylated CpG dinucleotides.

24. The method of claim 1, wherein the immunostimulatory nucleic acid is free of methylated CpG dinucleotides.

25. The method of claim 1, wherein the immunostimulatory nucleic acid is free of poly-C sequences.

26. The method of claim 1, wherein the immunostimulatory nucleic acid includes a poly-A sequence.

27. The method of claim 20, wherein the immunostimulatory nucleic acid includes a poly-G sequence.

28. The method of claim 1, wherein the immunostimulatory nucleic acid comprises a nucleotide composition of greater than 25% C.

29. The method of claim 1, wherein the immunostimulatory nucleic acid comprises a nucleotide composition of greater than 25% A.

30. The method of claim 1, wherein the immunostimulatory nucleic acid is administered orally.

31. The method of claim 1, wherein the immunostimulatory nucleic acid is administered locally.

32. The method of claim 1, wherein the immunostimulatory nucleic acid is administered in a sustained release device.

33. The method of claim 1, wherein the immunostimulatory nucleic acid is administered mucosally to a mucosal surface.

34. The method of claim 33, wherein the immune response is a mucosal immune response.

35. The method of claim 33, wherein the immune response is a systemic immune response.

36. The method of claim 33, wherein the mucosal surface is selected from the group consisting of an oral, nasal, rectal, vaginal, and ocular surface.

37. The method of claim 1, further comprising exposing the subject to an antigen and wherein the immune response is an antigen-specific immune response.

38. The method of claim 37, wherein a nucleic acid vector which encodes the antigen is administered to the subject, and wherein the nucleic acid vector is separate from the immunostimulatory nucleic acid.

39. The method of claim 37, wherein the antigen is a peptide antigen.

40. The method of claim 1, further comprising isolating an immune cell from the subject, contacting the immune cell with an effective amount to activate the immune cell of the immunostimulatory nucleic acid and re-administering the activated immune cell to the subject.

41. The method of claim 40, wherein the immune cell is a leukocyte.

42. The method of claim 41, further comprising contacting the immune cell with an antigen.

43. The method of claim 40, wherein the antigen is selected from the group consisting of a tumor antigen, a viral antigen, a bacterial antigen, and a parasitic antigen.

44. The method of claim 40, wherein the immune cell is a dendritic cell.

45. The method of claim 1, wherein the subject has or is at risk of developing asthma and the method is a method of treating or preventing asthma in the subject.

46. The method of claim 1, wherein the subject has or is at risk of developing allergy and the method is a method of treating or preventing allergy.

47. The method of claim 1, wherein the subject has cancer and the method is a method of treating the cancer.

48. The method of claim 47, wherein the cancer is selected from the group consisting of biliary tract cancer; brain cancer; breast cancer; cervical cancer; choriocarcinoma; CNS cancer, colon cancer; connective tissue cancer, endometrial cancer; eye cancer, gastric cancer; intraepithelial neoplasms; larynx cancer, lymphomas; Hodgkin's lymphoma, liver cancer; lung cancer (e.g. small cell and non-small cell); melanoma; neuroblastomas; oral cancer; oral cavity cancer, ovarian cancer; pancreas

cancer; prostate cancer; rectal cancer; sarcomas; thyroid cancer; and renal cancer, as well as other carcinomas and sarcomas.

49. The method of claim 1, wherein the cancer is selected from the group consisting of bone cancer, brain and CNS cancer, connective tissue cancer, esophageal cancer, eye cancer, Hodgkin's lymphoma, larynx cancer, oral cavity cancer, skin cancer, and testicular cancer.

50. The method of claim 47, further comprising administering an anti-cancer therapy.

51. The method of claim 50, wherein the anti-cancer therapy is an antibody.

52. The method of claim 47, wherein the subject is a human.

53. The method of claim 47, wherein the subject is selected from the group consisting of a dog, a cat, and a horse.

54. The method of claim 1, further comprising administering an antibody specific for a cell surface antigen, and wherein the immune response results in antigen dependent cellular cytotoxicity (ADCC).

55. The method of claim 1, wherein the subject has or is at risk of developing an infectious disease and wherein the method is a method for treating or preventing the infectious disease.

56. The method of claim 54, wherein the subject is a human.

57. The method of claim 54, further comprising administering an antigen to the subject.

58. The method of claim 57, wherein the antigen is selected from the group consisting of a bacterial antigen, a viral antigen, a parasitic antigen, and a fungal antigen.

59. The method of claim 56, wherein the subject is selected from the group consisting of a dog, cat, horse, cow, pig, sheep, goat, chicken, monkey, and fish.

60. The method of claim 59, further comprising administering an antigen to the subject.

61. The method of claim 59, wherein the antigen is derived from a microorganism selected from the group consisting of herpesviridae, retroviridae, orthomyroviridae, toxoplasma, haemophilus, campylobacter, clostridium, E.coli, and staphylococcus.

62. The method of claim 1, wherein the immunostimulatory nucleic acid is a TG nucleic acid.

63. The method of claim 62, wherein the TG nucleic acid comprises

$$5'N_1X_1TGX_2N_23'.$$

64. The method of claim 62, wherein the TG nucleic acid comprises

$$5'N_1X_1X_2TGX_3X_4N_23'.$$

65. The method of claim 63, wherein N_1 is a nucleic acid sequence composed of a number of nucleotides ranging from $(11\text{-}N_2)$ to $(21\text{-}N_2)$.

66. The method of claim 63, wherein N_2 is a nucleic acid sequence composed of a number of nucleotides ranging from $(11\text{-}N_1)$ to $(21\text{-}N_1)$.

67. The method of claim 64, wherein N_1 is a nucleic acid sequence composed of a number of nucleotides ranging from $(9\text{-}N_2)$ to $(19\text{-}N_2)$.

68. The method of claim 64, wherein N_2 is a nucleic acid sequence composed of a number of nucleotides ranging from $(9\text{-}N_1)$ to $(19\text{-}N_1)$.

69. The method of claim 63, wherein X_2 is thymidine.

70. The method of claim 64, wherein X_3 is thymidine.

71. The method of claim 64, wherein X_1X_2 are nucleotides selected from the group consisting of GT, GG, GA, AA, AT, AG, CT, CA, CG, TA and TT.

72. The method of claim 64, wherein X_3X_4 are nucleotides selected from the group consisting of TT, CT, AT, AG, CG, TC, AC, CC, TA, AA, and CA.

73. The method of claim 63, wherein X_3X_4 are nucleotides selected from the group consisting of TT, TC, TA and TG.

74. The method of claim 1, wherein the subject is at risk of developing cancer and the method is a method of preventing the cancer.

75. The method of claim 50, wherein the anti-cancer therapy is selected from the group consisting of a chemotherapeutic agent, an immunotherapeutic agent and a cancer vaccine.

76. A method for preventing disease in a subject, comprising:

administering to the subject an immunostimulatory nucleic acid on a regular basis to prevent disease in the subject, wherein the immunostimulatory nucleic acid is selected from the group consisting of a T-rich nucleic acid and a TG nucleic acid.

77. A method for inducing an innate immune response, comprising

administering to the subject an immunostimulatory nucleic acid in an amount effective for activating an innate immune response, wherein the immunostimulatory nucleic acid is selected from the group consisting of a T-rich nucleic acid and a TG nucleic acid.

78. A composition comprising

a sustained release device including an immunostimulatory nucleic acid, wherein the immunostimulatory nucleic acid is free of unmethylated CpG motifs and is selected from the group consisting of a T-rich nucleic acid and a TG nucleic acid.

79. The composition of claim 78, wherein the immunostimulatory nucleic acid has a phosphodiester backbone.

80. A composition of a nutritional supplement comprising

an immunostimulatory nucleic acid in a delivery device selected from the group consisting of a capsule, a pill, and a sublingual tablet, wherein the immunostimulatory nucleic acid is free of unmethylated CpG motifs and is selected from the group consisting of a T-rich nucleic acid and a TG nucleic acid.

81. The composition of claim 80, wherein the immunostimulatory nucleic acid has a phosphorothioate backbone.

82. A composition comprising
an immunostimulatory nucleic acid and an antigen, wherein the immunostimulatory nucleic acid is free of unmethylated CpG motifs and is selected from the group consisting of a T-rich nucleic acid and a TG nucleic acid.

83. A composition comprising
an immunostimulatory nucleic acid and an anti-microbial agent, wherein the immunostimulatory nucleic acid is free of unmethylated CpG motifs and is selected from the group consisting of a T-rich nucleic acid and a TG nucleic acid.

84. The composition of claim 83, wherein the anti-microbial agent is selected from the group consisting of an anti-viral agent, an anti-fungal agent, an anti-parasitic agent, and an anti-bacterial agent.

85. The method of claim 5, wherein the immunostimulatory nucleic acid comprises at least 3, at least 4, at least 5, at least 6, at least 7, or at least 8 T motifs.

86. The method of claim 5, wherein at least 2 of the plurality of poly T motifs each comprises at least three contiguous T nucleotide residues.

87. The method of claim 5, wherein at least two of the poly T motifs each comprises at least four contiguous T nucleotide residues.

88. The method of claim 5, wherein the plurality of poly T motifs is at least 3 motifs and wherein at least 3 motifs each comprises at least 3 contiguous T nucleotide residues.

89. The method of claim 5, wherein the plurality of poly T motifs is at least 4 motifs and wherein the at least 4 motifs each comprises at least 3 contiguous T nucleotide residues.

90. The method of claim 5, wherein at least one of the plurality of poly T motifs comprises at least 5, at least 6, at least 7, or at least 8 contiguous nucleotide residues.

91. The method of claim 1, wherein the immunostimulatory nucleic acid is free of two CpG dinucleotides.

92. The method of claim 1, wherein the immunostimulatory nucleic acid is free of three CpG dinucleotides.

93. The method of claim 1, wherein the immunostimulatory nucleic acid includes at least two poly C sequences of at least 3 contiguous C nucleotide residues.

94. The method of claim 1, wherein the immunostimulatory nucleic acid is free of two poly A sequences of at least 3 contiguous A nucleotide residues.

95. A pharmaceutical composition comprising an effective amount for stimulating an immune response of an isolated immunostimulatory nucleic acid of claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14,15, 16,17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 32, 40, 41, 64, 65, 66, 67, 68, 69, 70, 71, 72, 85, 86, 87, 88, 89, 90, 91, 92, 93, or 94 and a pharmaceutically acceptable carrier.

96. A composition of matter, comprising an isolated immunostimulatory nucleic acid of claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14,15, 16,17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 32, 40, 41, 64, 65, 66, 67, 68, 69, 70, 71, 72, 85, 86, 87, 88, 89, 90, 91, 92, 93, or 94 and a pharmaceutically acceptable carrier.

97 The method of claim 80 wherein the nucleic acid further comprises a plurality of CpG motifs, and wherein the plurality is at least 3 motifs, at least 4 motifs and wherein the at least 4 motifs each comprises at least 3 contiguous T nucleotide residues.

98 The method of claim 90 wherein the plurality of CpG motifs and poly T motifs are interspersed.

99. A composition, comprising:

an immunostimulatory nucleic acid and an anti-cancer therapy, formulated in a pharmaceutically-acceptable carrier and in an effective amount to treat a cancer or to reduce the risk of developing a cancer, wherein the immunostimulatory nucleic acid is selected from the group consisting of a T rich nucleic acid and a TG nucleic acid.

100. A composition, comprising:

an immunostimulatory nucleic acid and an asthma/allergy medicament, formulated in a pharmaceutically-acceptable carrier and in an effective amount for preventing or treating an immune response associated with exposure to a mediator of asthma or allergy, wherein the immunostimulatory nucleic acid is selected from the group consisting of a T-rich nucleic acid, a TG nucleic acid and a C-rich nucleic acid.

101. A composition comprising

an immunostimulatory nucleic acid selected from the group consisting of SEQ ID NO: 95-136, SEQ ID NO: 138-152, SEQ ID NO: 154-222, SEQ ID NO: 224-245, SEQ ID NO: 247-261, SEQ ID NO: 263-299, SEQ ID NO: 301, SEQ ID NO: 303-4109, SEQ ID NO: 414-420, SEQ ID NO: 424, SEQ ID NO: 426-947, SEQ ID NO: 959-1022, SEQ ID NO: 1024-1093, and a pharmaceutically acceptable carrier.

102. A composition comprising

an immunostimulatory nucleic acid consisting essentially of:

5' M_1TCGTCGTTM_2 3'

wherein at least one of the Cs is unmethylated, wherein M_1 is a nucleic acid having at least one nucleotide, wherein M_2 is a nucleic acid having between 0 and 50 nucleotides, and wherein the immunostimulatory nucleic acid has less than 100 nucleotides.

103. A pharmaceutical composition comprising

an immunostimulatory nucleic acid comprising:

5' TCGTCGTT 3'

wherein at least one of the Cs is unmethylated, wherein the immunostimulatory nucleic acid has less than 100 nucleotides and a phosphodiester backbone, and

a sustained release device.

104. The pharmaceutical composition of claim 103 wherein the sustained release device is a microparticle.

105. The pharmaceutical composition of claim 103, further comprising an antigen.

106. An assay for identifying an adjuvant,

contacting an NK cell preparation with a putative adjuvant, measuring NK cell activity, and comparing the level of NK cell activation with a control to determine whether the putative adjuvant is an effective adjuvant.